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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/682,562	09/20/2001	Nancy T. Chang	TNX00-08	1390

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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	4

DATE MAILED: 10/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary

Application No.	Applicant(s)
09/682,562	Chang et al
Examiner	**Art Unit**
Jane Zara	1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Sep 24, 2001* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-9* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-9 are pending in the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, line 5, the abbreviation ISO should be spelled out (e.g. replacing "ISO" with --immune stimulatory oligonucleotide-- would perhaps be remedial).

In claim 2, line 3, the metes and bounds of "at least at position C-5 of the cytosine in the CpG sequence" cannot be determined (e.g. Does this mean it would go in another C position of the cytosine, or somewhere on the G portion of the CpG?). Appropriate clarification is requested.

In claim 5, line 2, "the subject" lacks proper antecedent basis.

In claim 8, line 1, "claims 5" is unclear (perhaps replacing "claims" with --claim-- would be remedial).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang in view of Carson et al, the combination in view of Schwartz and Idusogie et al.

The claims are drawn to a method of stimulating antibody dependent cellular cytotoxicity in a mammal including a human, to enhance the elimination of IgE-bearing B cells comprising administration of a CpG containing oligonucleotide comprising an electron-withdrawing group at C-5 of cytosine in the CpG sequence, in combination with the administration of an anti-IgE antibody that binds to membrane bound IgE, but does not induce histamine release, which anti-IgE antibody is E27, or optionally comprises a human IgG1 Fc portion, and which CpG containing oligonucleotide comprises SEQ ID NO: 1, 2, 3 or 4, and which CpG containing oligonucleotide is administered in combination with a conjugated allergen.

Chang (USPN 5,614,611) teaches a method of stimulating antibody dependent cellular cytotoxicity (ADCC) to enhance the elimination of IgE bearing B cells comprising administration to a mammal including a human anti IgE antibody that binds to membrane bound IgE but does not

induce histamine release, which anti IgE antibody has a human IgG, IgG3 Fc or mouse IgG2a Fc region (col. 4, line 8- col. 5, line 11).

Chang does not teach the co-administration of CpG containing oligonucleotides in stimulating ADCC to enhance the elimination of IgE bearing B cell, nor the incorporation of electron-withdrawing groups into the CpG sequence, nor the co-administration of a conjugated allergen with the CpG containing oligonucleotide, which CpG containing oligonucleotide comprises either SEQ ID NO: 1, 2, 3 or 4. Nor does Chang teach the anti IgE antibody of E25, 26 or 27, not Hu-901.

Carson et al teach the administration of a CpG containing oligonucleotides in combination with a conjugated allergen to a mammal including a human, wherein a shift from a Th2 to a Th1 immune response is obtained in the mammal and unwanted IgE side effects are reduced (see col. 3-5, and example 11 in col. 19).

Schwartz teaches the administration of CpG containing oligonucleotides, which comprise electron-withdrawing groups at least at C-5 of cytosine in the CpG sequence (col. 1, lines 19-25; col. 4, lines 13-21), and which CpG containing oligonucleotides comprise SEQ ID NO. 1,2, 3 or 4, col. 7, lines 48-62).

Idusogie et al teach human chimeric anti IgE antibodies for decreasing IgE-bearing B cells, Idusogie et al teach the anti IgE antibody E27 (figure 4; col. 15, lines 31-47; claim 5).

It would have been obvious to one of ordinary skill in the art to enhance the elimination of IgE bearing B cells comprising administration of an anti IgE antibody that binds to membrane

bound IgE, but does not induce histamine release because Chang has taught this method to eliminate IgE bearing B cells in a mammal. One of ordinary skill in the art would have further reduced IgE associated side effects in a mammal comprising the co-administration of a CpG containing oligonucleotide further comprising a conjugated antigen because Carson et al teach the administration of CpG containing oligonucleotides with conjugated antigen to shift from a Th2 to a Th1 associated immune response in an organism, thereby suppressing undesirable IgE side effects such as anaphylaxis. One of ordinary skill in the art would have expected that the co-administration of an anti IgE antibody and a CpG containing oligonucleotide with conjugated antigen would diminish IgE bearing B cells in the organism, thereby reducing IgE immune effects such as anaphylaxis. One of ordinary skill in the art would have been motivated to incorporate an electron-withdrawing group into the cytosine component of the CpG containing oligonucleotide, including SEQ ID NOS. 1, 2, 3 and 4, because Schwartz has taught that the incorporation of electron-withdrawing residues into the cytosine residue of these sequences enhances the desired immunomodulatory effects of a CpG oligonucleotide (e.g. see Schwartz at col. 25), including the eventual suppression of IgE mediated side effects such as anaphylaxis. One of ordinary skill in the art would have expected that the administration of CpG oligonucleotides, containing such a modified cytosine, would enhance the elimination of IgE bearing B cells. One of ordinary skill in the art would have been motivated to administer human chimeric anti IgE antibodies because these antibodies have been shown by Idusogie et al to retain high affinity for the IgE antibody, while minimizing unwanted antigenic or immune responses that are elicited in humans using non-

chimeric mouse antibodies. One of ordinary skill in the art would have expected that the administration of a human chimeric anti-IgE antibody, in combination with a CpG containing oligonucleotide of SEQ ID NO. 1, 2 3 or 4, and further comprising a conjugated antigen, and which oligonucleotide also comprises an electron-withdrawing group on the cytosine of the CpG component of the oligonucleotide, would reduce unwanted IgE related immune effects in a human, such as anaphylaxis, by eliminating IgE bearing B cells in the organism, as well as shifting from a Th2 to a Th1 immune response.

Therefore, the invention as a whole would have prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to

reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER

JZ

September 27, 2003